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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/617,616	07/11/2003	Bore G. Raju	PC19348A	2915

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PFIZER INC.
PATENT DEPARTMENT, MS8260-1611
GROTON, CT 06340

EXAMINER	
LOEWE, SUN JAE Y	
ART UNIT	PAPER NUMBER
1626	

NOTIFICATION DATE	DELIVERY MODE
05/15/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

~IPGSGro@pfizer.com

Office Action Summary	Application No.	Applicant(s)	
	10/617,616	RAJU ET AL.	
	Examiner	Art Unit	
	SUN JAE Y. LOEWE	1626	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 April 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-31* is/are pending in the application.

4a) Of the above claim(s) *3,4,6-8,12 and 20-30* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,5,9-11,14-19 and 31* is/are rejected.

7)☒ Claim(s) *13* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *1-9-2008;9-17-2004;3-11-2004*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

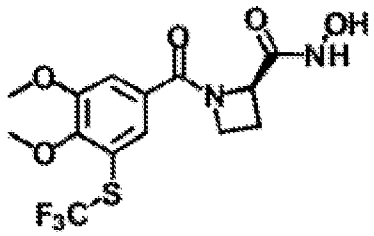
DETAILED ACTION

1. Claims 1-31 are pending in the instant application.

Election/Restrictions

2. Applicant's election without traverse of Group I in the reply filed on April 1, 2008 is acknowledged. The restriction requirement between Groups I and II is hereby made FINAL.

3. Applicant's election of the species below in the reply filed on April 1, 2008 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the election of species requirement, the election is treated as an election without traverse (MPEP § 818.03(a)).



4. MPEP § 803.02 provides guidelines for election of species in Markush-type claims:

> "Markush-type claim will be examined fully with respect to the elected species and further to the extent necessary to determine patentability. If the Markush-type claim is not allowable **, the provisional election will be given effect and examination will be limited to the Markush-type claim and claims to the elected species, with claims drawn to species patentably distinct from the elected species held withdrawn from further consideration. "

The elected species appeared to be allowable over the prior art. However, the Markush-type claims encompassing the elected species was not allowable (Sections 7-11). Thus, the provisional election of species was given effect and non-elected subject matter (ie. all non-elected compounds encompassed by Formulas I-III) withdrawn from further consideration.

5. Claims 3, 4, 6-8, 12 and 20-30 withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected subject matter. Applicant elected without traverse in the response dated April 1, 2008.

Information Disclosure Statement

6. The information disclosure statements (dated March 11, 2004; September 17, 2004; January 9, 2008) were in compliance with the provisions of 37 CFR 1.97 and 37 CFR 1.98. The statements were considered. The crossed out references were not considered because copies were not provided. Signed forms 1449 enclosed herewith.

Claim Objections

7. Claims 1, 2, 5, 9-11, 13-19 and 31 objected to for containing non-elected subject matter.

8. Claim 13 objected to because it is not written in proper Markush format. Applicant is requested to add the term "and" between the entries of

1-(4-benzyloxy-3-trifluoromethylthiobenzoyl)-azetidine-2R-carboxylic acid hydroxyamide; and

1-(3,4-dimethoxy-5-trifluoromethylthiobenzoyl)-4,4-difluoropyrrolidine-2R-carboxylic acid hydroxyamide;

Applicant is further requested to replace the term "and" with the term "or" in the following: and pharmaceutically acceptable salts thereof as well as any and all tautomers thereof.

9. Claims 1 and 13 objected to for not being written in proper alternative form. The following correction is suggested to overcome this ground of objection: replace „ and pharmaceutically acceptable salts thereof as well as any and all tautomers thereof " with "or a pharmaceutically acceptable salt or tautomer thereof."

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. Claims 1, 2, 5, 9-11, 13-19 and 31 rejected under 35 USC 112 1st paragraph as failing to comply with the written description requirement.

The MPEP states that the purpose of the written description requirement is to ensure that the inventor had possession, as of the filing date of the application, of the specific subject matter later claimed by him. The courts have stated:

> "To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (Fed. Cir. 1997); In re Gostelli, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) ("[T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant

> complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." Lockwood, 107 F.3d at 1572, 41 USPQ2d at 1966." Regents of the University of California v. Eli Lilly & Co., 43 USPQ2d 1398.

Further, for a broad generic claim, the specification must provide adequate written description to identify the genus of the claim. In *Regents of the University of California v. Eli Lilly & Co.* the court stated:

> "A written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." *Fiers*, 984 F.2d at 1171, 25 USPQ2d 1601; *In re Smythe*, 480 F.2d 1376, 1383, 178 USPQ 279, 284985 (CCPA 1973) ("In other cases, particularly but not necessarily, chemical cases, where there is unpredictability in performance of certain species or subcombinations other than those specifically enumerated, one skilled in the art may be found not to have been placed in possession of a genus …") *Regents of the University of California v. Eli Lilly & Co.*, 43 USPQ2d 1398.

The MPEP states that for a generic claim the genus can be adequately described if the disclosure presents a sufficient number of representative species that encompass the genus. MPEP § 2163. If the genus has a substantial variance, the disclosure must describe a sufficient variety of species to reflect the variation within that genus. See MPEP § 2163. Although the MPEP does not define what constitute a sufficient number of representative species, the courts have indicated what do not constitute a representative number of species to adequately describe a broad genus. In *Gostelli*, the courts determined that the disclosure of two chemical compounds within a subgenus did not describe that subgenus. *In re Gostelli*, 872, F.2d at 1012, 10 USPQ2d at 1618.

The Guidelines for Examination of Patent Applications Under 35 USC 112, ¶1, "Written Description" Requirement (Federal Register, Vol. 66, No. 4, pg. 1105, column 3), in accordance with MPEP § 2163, specifically state that for each claim drawn to a genus the written description requirement may be satisfied through sufficient description of a representative number of species by a) actual reduction to practice; b) reduction to

drawings or structural chemical formulas; c) disclosure of relevant, identifying characteristics (ie. structure) by functional characteristics coupled with a known or disclosed correlation between function and structure. The analysis of whether the specification complies with the written description requirement calls for the examiner to compare the scope of the claim with the scope of the description to determine whether applicant has demonstrated possession of the claimed invention (Federal Register, Vol. 66, No. 4, p. 1105, 3rd column, 3rd paragraph). Below is such comparison.

I. ***Scope of Claims***

Compounds of Formula I.

The following variables are claimed *broader* than what is supported by the disclosure (see below section II):

R^1/R^2:	all claims
X^1-X^4:	all claims *except* claim 10
Ar:	all claims *except* claims 9 and 10

II. ***Scope of Disclosure***

Reduction to Practice:

The compounds reduced to practice support the following definitions for the variables

R^1/R^2:	hydrogen, alkyl;
X^1-X^4:	hydrogen, alkyl, haloalkyl, alkylthio, alkylsulfinyl, alkylsulfonyl, hydroxyalkyl, alkoxy, alkoxyalkyl, haloalkoxy, alkenyl, alkenoxy, alkenoxyalkyl, alkynyl, alkynyloxy, nitro, halo, hydroxy, cycloalkyl, haloalkylthio, haloalkylsulfinyl, haloalkylsulfonyl, alkylsilylalkynyl, alkynyloxy, anaminocarbonylalkyl, carboxylate, carboxyl, carboxamide;
Ar:	phenyl and 2,5-dihydro-benzo[b]oxepine

Reduction to Structural or Chemical Formulas:

There is no disclosure of species (eg. by reduction to structural/chemical formulas) in addition to those reduced to practice.

Correlation between Structure and Function:

Structure-activity studies (SAR) are disclosed in the art for antibacterial compounds with core structures different from those instantly claimed. Although these studies do not address the activity of the compounds of the instant genus as a function of structural modifications, they do show that a compound's ability to retain the activity is affected by structural changes to the common chemical core (eg. see below section 11). Because instant specification does not disclose a correlation between function and structure, and because such correlation is not commonly known in the art, one of ordinary skill would not know what *specific structural elements* would allow for preservation of activity within the unrepresented genus.

III. *Analysis of Fulfillment of Written Description Requirement:*

In the absence of a correlation between structure and function, it is not possible to know what modifications to the instantly claimed core structure will allow for the preservation of the desired activity.

In conclusion: (i) substantial structural variation exists in the genus/subgenus embraced by claims 1, 2, 5, 9-11, 13-19 and 31; (ii) disclosure of species supporting genus is limited to compounds reduced to practice, which scope is not commensurate with the scope of genus/subgenus claimed; (iii) common structural attributes of the claimed genus/subgenus, combined with a correlation between structure and function, is neither disclosed in the instant application nor commonly known in the art. Thus, the specification fails to provide adequate written description for the genus of compounds claimed and does not reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the entire scope of the claimed invention.

(Enablement)

11. Claims 1, 2, 5, 9-11, 13-19 and 31 rejected under 35 U.S.C. 112, first paragraph. The specification is enabling for making and using compounds that have adequate written description. The specification is not enabling for using compounds that are not supported by the disclosure. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with the claims.

The standard for determining whether the specification meets the enablement requirement was cast in the Supreme Court decision of *Mineral Separation v. Hyde*, 242 U.S. 261, 270 (1916) which postured the question: is the experimentation needed to practice the invention undue or unreasonable? That standard is still the one to be applied. *In re Wands*, 858 F.2d 731, 737, 8USPQ2s 1400, 1404 (Fed. Cir. 1988). MPEP 2164.01(a) states "There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is undue". The factors are applied below to the instant claims.

The breadth of the claims
Claims drawn to compounds that *do not* have written description support.

The nature of the invention
The compounds are disclosed to be antibacterial. Additional utility is neither disclosed nor known in the art.

The state of the prior art/level of ordinary skill/level of predictability
The level of ordinary skill is high, but the level of predictability in the art is low. The antibacterial activity of a compound is dependent on structural parameters. It is well documented in the art that changes to the structure/chemical properties of a compound can have unpredictable

results on its overall antibacterial activity. For example, see disclosure of Belgodere et al., excerpts below:

Table 8: In vitro tests of 1-alkylaryl imidazole-5-carbohydrazonic acids. (MIC in μg/ml).

	Medium	Ia	Ia HCl	Ib	Ib HCl	Id	Ie
Bacillus subtilis ATCC 9466	BHI Agar	>100	11		3.3		25
Staphylococcus aureus SMITH			100	50	12	200	>100
Staphylococcus aureus CIP (res. Pen.)			>100		50		
Staphylococcus aureus 6814668 (res. Met.)			100			200	
Streptococcus pyogenes haemolyticus C 203			>100		100	>200	25
Streptococcus faecalis ATCC 6057							>100
Escherichia coli 120			100		25	25	
Salmonella typhimurium					100		
Shigella dysenteriae NCTC 4837			>100			100	
Shigella sonnei ATCC 11060				200			
Klebsiella pneumoniae ATCC 10031			100	3.1	3.1	12.5	25
Pseudomonas aeruginosa ATCC 9027				200	100	>200	>100
Proteus vulgaris 20			>100				
Candida albicans 3965				>200	>100		
Candida albicans ATCC 2091							
Saccharomyces cerevisiae ATCC 7921							
Aspergillus niger NRRL 3							
Clostridium bifermentans	Thiogl.			25	3.7	>100	50
Clostridium sporogenes			100	100	100		>100
Entamoeba histolytica MEAH	Jones			>100	>100		
Trichomonas vaginalis	Thiogl.			100	100		

Example above provided to illustrate inability to predict activity.

As discussed in section 10, it is not known what specific structural changes are tolerated for producing active antibacterial compounds. One of ordinary skill could not predict which of the structurally diverse compounds, embraced by the claims but not exemplified/supported by the disclosure, would possess the desired activity. Lacking use as antibacterial agents, in view of the absence of an alternate reported utility, one of ordinary skill is not enabled by the disclosure to use the compounds which do not have written description support.

The amount of direction provided by the inventor/existence of working examples
Direction and working examples limited to the compounds that are adequately represented by the disclosure (Section 10.II).

The quantity of experimentation needed to make or use the invention
It would require undue experimentation for one of ordinary skill to practice the invention commensurate in scope with the breadth of the instant claims.

Conclusion

12. No claims allowed.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sun Jae Y. Loewe whose telephone number is (571) 272-9074. The examiner can normally be reached on M-F 7:30-5:00 Est.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph McKane can be reached on (571)272-0699. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Sun Jae Y. Loewe, Ph.D./
5-5-2008

/Kamal A Saeed, Ph.D./
Primary Examiner, Art Unit 1626